IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Fumihide NISHIO

Confirmation No. 9947

Serial No. 10/501,671
    (PCT/JP03/00339)

PCT/DO/EO

Filed July 16, 2004

HIGH-CONCENTRATION PREPARATION
OF SOLUBLE THROMBOMODULIN

RESPONSE TO NOTIFICATION OF MISSING REQUIREMENTS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA   22313-1450

June 28, 2005

Sir:

In response to the accompanying Notification of Missing Requirements under 35 U.S.C. § 371 mailed March 31, 2005, we enclose herewith the executed Declaration, which was omitted at the time of filing the application. The required 37 C.F.R. § 1.492(e) surcharge was paid at the time of filing the application. Also enclosed is a Supplemental Application Data Sheet.

Attached herewith is a Statement to Support Filing and

Submission in Accordance with 37 C.F.R. §§ 1.821-1.825 with the

Sequence Listing in paper and disk formats.

Respectfully submitted,

YOUNG & THOMPSON

Michael Piziali, Reg. No. 46,997
745 South 23rd Street
Arlington, VA 22202
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MP:fb

UNITED STATES PATENT AND TRADEMARK OFFICE

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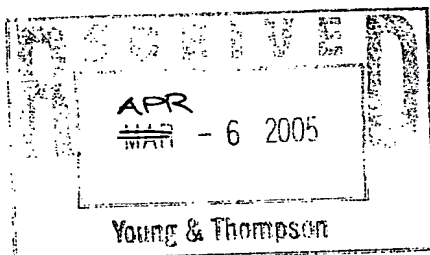Alexandria, Virginia 22313-1450
www.uspto.gov

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
10/501,671	Fumihide Nishio	8062-1023

INTERNATIONAL APPLICATION NO.		
PCT/JP03/00339		
I.A. FILING DATE	PRIORITY DATE	
01/17/2003	01/18/2002	

00466
YOUNG & THOMPSON
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APR - 6 2005
Young & Thompson

CONFIRMATION NO. 9947
371 FORMALITIES LETTER
OC000000015512526

Date Mailed: 03/31/2005

NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495).

- Copy of the International Application filed on 07/16/2004
- Copy of the International Search Report filed on 07/16/2004
- Copy of IPE Report filed on 07/16/2004
- Preliminary Amendments filed on 07/16/2004
- Information Disclosure Statements filed on 07/16/2004
- Biochemical Sequence Diskette filed on 07/16/2004
- Biochemical Sequence Listing filed on 07/16/2004
- Request for Immediate Examination filed on 07/16/2004
- Copy of references cited in ISR filed on 07/16/2004
- U.S. Basic National Fees filed on 07/16/2004
- Priority Documents filed on 07/16/2004

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date.

- This application clearly fails to comply with the requirements of 37 CFR. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000). Applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper or compact disc copy of the "Sequence Listing", as well as an amendment directing its entry into the application. Applicant must also

provide a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). If applicant desires the sequence listing in the instant application to be identical with that of another application on file in the U.S. Patent and Trademark Office, such request in accordance with 37 CFR 1.821(e) may be submitted in lieu of a new CRF.

- This application does not contain a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). Applicant must provide such statement. If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000).

ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

For questions regarding compliance to 37 CFR 1.821-1.825 requirements, please contact:

- **For Rules Interpretation, call (571) 272-0951**
- **For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.**
- **Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov**

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)
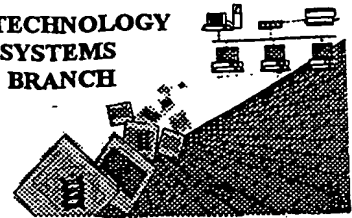
*A copy of this notice **MUST** be returned with the response.*

CHRISTINE S WASHINGTON

Telephone: (703) 308-9140 EXT 228

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/501,671	PCT/JP03/00339	8062-1023

FORM PCT/DO/EO/905 (371 Formalities Notice)

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: *10/501,671*

Source: *PCT/10*

Date Processed by STIC: *7/23/04*

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY
FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE <u>CHECKER VERSION 4.2 PROGRAM</u>, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 06/05/04): U.S. Patent and Trademark Office, 220 20th Street S.; Customer Window, Mail Stop Sequence, Crystal Plaza Two, Lo Room 1B03, Arlington, VA 22202

Revised 05/17/04

Raw Sequence Listing Error Summary

ERROR DETECTED   SUGGESTED CORRECTION   SERIAL NUMBER: *10/501,671*

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1 ____ Wrapped Nucleics   The number/text at the end of each line "wrapped" down to the next line. This may occur if your file
     Wrapped Aminos   was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will
                      prevent "wrapping."

2 ____ Invalid Line Length   The rules require that a line not exceed 72 characters in length. This includes white spaces.

3 ____ Misaligned Amino   The numbering under each 5ᵗʰ amino acid is misaligned. Do not use tab codes between numbers;
     Numbering   use space characters, instead.

4 ____ Non-ASCII   The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please
                      ensure your subsequent submission is saved in ASCII text.

5 ____ Variable Length   Sequence(s)____contain n's or Xaa's representing more than one residue. Per Sequence Rules,
                      each n or Xaa can only represent a single residue. Please present the maximum number of each
                      residue having variable length and indicate in the <220>-<223> section that some may be missing.

6 ____ PatentIn 2.0   A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid
     "bug"   sequences(s) _____. Normally, PatentIn would automatically generate this section from the
                      previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to
                      the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for
                      Artificial or Unknown sequences.

7 ____ Skipped Sequences   Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence:
     (OLD RULES)   (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
                  (i)   SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
                  (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
                  This sequence is intentionally skipped

                  Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

8 ____ Skipped Sequences   Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence.
     (NEW RULES)   <210> sequence id number
                  <400> sequence id number
                  000

9 ____ Use of n's or Xaa's   Use of n's and/or Xaa's have been detected in the Sequence Listing.
     (NEW RULES)   Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
                  In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

10 ____ Invalid <213>   Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or
     Response   scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or
                  is Artificial Sequence

11 ____ Use of <220>   Sequence(s) _____ missing the <220> "Feature" and associated numeric identifiers and responses.
                  Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or
                  "Unknown." Please explain source of genetic material in <220> to <223> section.
                  (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32)   (Sec. 1.823 of Sequence Rules)

12 ____ PatentIn 2.0   Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file,
     "bug"   resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence
                  listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

13 ____ Misuse of n/Xaa   "n" can only represent a single <u>nucleotide</u>; "Xaa" can only represent a single <u>amino acid</u>

AMC – Biotechnology Systems Branch – 09/09/2003

PCT

```
        3 <110> APPLICANT: Asahi Kasei Kabushiki Kaisha
W-->    4 <120> TITLE OF INVENTION: High-concentration preparation of soluble thrombomodulin
        6 <130> FILE REFERENCE: ASAHI-33
C-->    8 <140> CURRENT APPLICATION NUMBER: US/10/501,671
C-->    8 <141> CURRENT FILING DATE: 2004-07-16
        8 <150> PRIOR APPLICATION NUMBER: JP2002-009951
        9 <151> PRIOR FILING DATE: 2002-01-18
       11 <160> NUMBER OF SEQ ID NOS: 9
```

pp 1-6

Does Not Comply
Corrected Diskette Needed

ERRORED SEQUENCES

```
       13 <210> SEQ ID NO: 1
       14 <211> LENGTH: 516
       15 <212> TYPE: PRT
       16 <213> ORGANISM: Artificial sequence
       18 <220> FEATURE:
       19 <223> OTHER INFORMATION: Partial amino acid sequence of human-originated soluble
       20       thrombomodulin
       22 <400> SEQUENCE: 1
       23 Met Leu Gly Val Leu Val Leu Gly Ala Leu Ala Leu Ala Gly Leu Gly
E-->   24  1               5               10              10      15
       25 Phe Pro Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu
E-->   26          20      20              25      25      30      30
       27 His Asp Cys Phe Ala Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala
E-->   28          35                      40                      45
       29 Ser Gln Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser
E-->   30          50                      55                      60
       31 Ser Val Ala Ala Asp Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly
E-->   32  65                      70                      75              80
       33 Val Gly Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys
E-->   34                  85                      90                      95
       35 Gly Asp Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr
E-->   36                  100                     105                     110
       37 Gly Asp Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn
E-->   38                  115                     120                     125
       39 Gly Ala Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu
E-->   40                  130                     135                     140
       41 Ala Thr Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val
E-->   42  145                     150                     155                     160
       43 Lys Ala Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg
E-->   44                  165                     170                     175
       45 Pro Leu Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr
```

misaligned amino acid number
15 (see item 3 on Error summary Sheet)

see p. 2

RAW SEQUENCE LISTING   DATE: 07/23/2004
PATENT APPLICATION: US/10/501,671   TIME: 15:23:45

Input Set : A:\PTO.FG.txt
Output Set: N:\CRF4\07232004\J501671.raw

```
E--> 46              180                    185                190    Same
     47 Tyr Gly Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro    error
E--> 48              195                    200                205
     49 Val Gly Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys
E--> 50        210                    215                220
     51 Thr Ala Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro
E--> 52 225                    230                    235                240
     53 Gly Ala Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys
E--> 54              245                    250                255
     55 Asn Ala Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala
E--> 56              260                    265                270
     57 Leu Gln Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys
E--> 58         275                    280                    285
     59 Asn Asp Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly
E--> 60        290                    295                300
     61 Ser Tyr Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln
E--> 62 305                    310                    315                320
     63 His Arg Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys
E--> 64              325                    330                335
     65 Pro Gln Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr
E--> 66              340                    345                350
     67 Pro Asn Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro
E--> 68         355                    360                    365
     69 Cys Phe Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr
E--> 70        370                    375                380
     71 Ser Tyr Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu
E--> 72 385                    390                    395                400
     73 Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp
E--> 74              405                    410                415
     75 Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile
E--> 76              420                    425                430
     77 Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly
E--> 78              435                    440                445
     79 Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys
E--> 80        450                    455                460
     81 Ile Cys Gly Pro Asp Ser Ala Leu Val Arg His Ile Gly Thr Asp Cys
E--> 82 465                    470                    475                480
     83 Asp Ser Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro
E--> 84              485                    490                495
     85 Pro Ser Pro Thr Pro Gly Ser Thr Leu Thr Pro Pro Ala Val Gly Leu
E--> 86              500                    505                510
     87 Val His Ser Gly
E--> 88              515
     90 <210> SEQ ID NO: 2  1547 (p.3)
     91 <211> LENGTH: 1548
     92 <212> TYPE: DNA
     93 <213> ORGANISM: Artificial sequence
     95 <220> FEATURE:
     96 <223> OTHER INFORMATION: Partial base sequence of human-originated soluble
```

RAW SEQUENCE LISTING   DATE: 07/23/2004
PATENT APPLICATION: US/10/501,671   TIME: 15:23:45

Input Set : A:\PTO.FG.txt
Output Set: N:\CRF4\07232004\J501671.raw

```
97          thrombomodulin gene
99  <400> SEQUENCE: 2
100  atgcttgggg tcctggtcct tggcgcgctg gccctggccg gcctggggtt ccccgcaccc    60
101  gcagagccgc agccgggtgg cagccagtgc gtcgagcacg actgcttcgc gctctacccg   120
102  ggccccgcga ccttcctcaa tgccagtcag atctgcgacg gactgcgggg ccacctaatg   180
103  acagtgcgct cctcggtggc tgccgatgtc atttccttgc tactgaacgg cgacggcggc   240
104  gttggccgcc ggcgcctctg gatcggcctg cagctgccac ccggctgcgg cgaccccaag   300
105  cgcctcgggc ccctgcgcgg cttccagtgg gttacgggag acaacaacac cagctatagc   360
106  aggtgggcac ggctcgacct caatggggct cccctctgcg cccgttgtg cgtcgctgtc    420
107  tccgctgctg aggccactgt gcccagcgag ccgatctggg aggagcagca gtgcgaagtg   480
108  aaggccgatg gcttcctctg cgagttccac ttcccagcca cctgcaggcc actggctgtg   540
109  gagcccggcg ccgcggctgc cgccgtctcg atcacctacg caccccgtt cgcggcccgc    600
110  ggagcggact ccaggcgct gccggtgggc agctccgccg cggtggctcc cctcggctta    660
111  cagctaatgt gcaccgcgcc gcccggagcg gtccaggggc actgggccag ggaggcgccg   720
112  ggcgcttggg actgcagcgt ggagaacggc ggctgcgagc acgcgtgcaa tgcgatccct   780
113  ggggctcccc gctgccagtg cccagccggc ccgcccctgc aggcagacgg cgcgctcctgc  840
114  accgcatccg cgacgcagtc ctgcaacgac ctctgcgagc acttctgcgt tcccaacccc   900
115  gaccagccgg gctcctactc gtgcatgtgc gagaccggct accggctggc ggccgaccaa   960
116  caccggtgcg aggacgtgga tgactgcata ctggagccca gtccgtgtcc gcagcgctgt  1020
117  gtcaacacac agggtggctt cgagtgccac tgctacccta actacgacct ggtggacggc  1080
118  gagtgtgtgg agcccgtgga cccgtgcttc agagccaact gcgagtacca gtgccagccc  1140
119  ctgaaccaaa ctagctacct ctgcgtctgc gccgagggct cgcgcccat tccccacgag  1200
120  ccgcacaggt gccagatgtt ttgcaaccag actgcctgtc cagccgactg cgaccccaac  1260
121  acccaggcta gctgtgagtg ccctgaaggc tacatcctgg acgacggttt catctgcacg  1320
122  gacatcgacg agtgcgaaaa cggcggcttc tgctccgggg tgtgccacaa cctccccggt  1380
E--> 123  accttcgagt gcatctgcgg gcccgactcg gcccttgtcc gccacattgg (caccgac)(1440)/1439
E--> 124  gactccggca aggtggacgg tggcgacagc ggctctggcg agcccccgcc (cagcccgacg)(1500)/1499
E--> 125  cccggctcca ccttgactcc tccggccgtg gggctcgtgc attcgggc                1547 (1548)
127  <210> SEQ ID NO: 3
128  <211> LENGTH: 132
129  <212> TYPE: PRT
130  <213> ORGANISM: Artificial sequence
132  <220> FEATURE:
133  <223> OTHER INFORMATION: Partial amino acid sequence of human-originated soluble
134        thrombomodulin
E--> 136  <400> SEQUENCE: (8)3  ← change to
137  Met Leu Gly Val Leu Val Leu Gly Ala Leu Ala Leu Ala Gly Leu Gly
E--> 138   1              5                    10                      15
139  Phe Pro Asp Pro Cys Phe Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro
E--> 140               20                   25              30
141  Leu Asn Gln Thr Ser Tyr Leu Cys Val Cys Ala Glu Gly Phe Ala Pro
E--> 142              35                   40                  45
143  Ile Pro His Glu Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala
E--> 144           50                   55                   60
145  Cys Pro Ala Asp Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro
E--> 146  (65                  70                   75                      80
147  Glu Gly Tyr Ile Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu
E--> 148               85                   90                      95
149  Cys Glu Asn Gly Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly
```

(handwritten annotations:)

FYI: periods are invalid nucleic acid designation.

This is a group of 9 positions, not 10.

misaligned amino acid numbers

RAW SEQUENCE LISTING   DATE: 07/23/2004
PATENT APPLICATION: US/10/501,671   TIME: 15:23:45

Input Set : A:\PTO.FG.txt
Output Set: N:\CRF4\07232004\J501671.raw   *misaligned numbers*

E--> 150   100   105   110
     151 Thr Phe Glu Cys Ile Cys Gly Pro Asp Ser Ala Leu Val Arg His Ile
E--> 152   115   120   125
     153 Gly Thr Asp Cys
E--> 154   130
     174 <210> SEQ ID NO: 5
     175 <211> LENGTH: 516
     176 <212> TYPE: PRT
     177 <213> ORGANISM: Artificial sequence
     179 <220> FEATURE:
     180 <223> OTHER INFORMATION: Partial amino acid sequence of human-originated soluble
     181   thrombomodulin
     183 <400> SEQUENCE: 5
     184 Met Leu Gly Val Leu Val Leu Gly Ala Leu Ala Leu Ala Gly Leu Gly
E--> 185 1   5   10   15
     186 Phe Pro Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu   *misaligned*
E--> 187   20   25   30   *amino acid*
     188 His Asp Cys Phe Ala Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala   *number*
E--> 189   35   40   45
     190 Ser Gln Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser
E--> 191   50   55   60
     192 Ser Val Ala Ala Asp Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly
E--> 193 65   70   75   80
     194 Val Gly Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys
E--> 195   85   90   95
     196 Gly Asp Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr
E--> 197   100   105   110
     198 Gly Asp Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn
E--> 199   115   120   125
     200 Gly Ala Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu
E--> 201   130   135   140
     202 Ala Thr Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val
E--> 203 145   150   155   160
     204 Lys Ala Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg
E--> 205   165   170   175
     206 Pro Leu Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr
E--> 207   180   185   190
     208 Tyr Gly Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro
E--> 209   195   200   205
     210 Val Gly Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys
E--> 211   210   215   220
     212 Thr Ala Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro
E--> 213 225   230   235   240
     214 Gly Ala Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys
E--> 215   245   250   255
     216 Asn Ala Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala
E--> 217   260   265   270
     218 Leu Gln Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys
E--> 219   275   280   285

P.5

```
    220 Asn Asp Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly      same
E--> 221      290                     295                     300            err
    222 Ser Tyr Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln
E--> 223 305                     310                     315                     320
    224 His Arg Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys
E--> 225                      325                     330                     335
    226 Pro Gln Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr
E--> 227                      340                     345               350
    228 Pro Asn Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro
    229           355                     360                     365
    230 Cys Phe Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr
E--> 231           370                     375                     380
    232 Ser Tyr Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu
E--> 233 385                     390                     395                     400
    234 Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp
E--> 235                      405                     410                     415
    236 Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile
E--> 237                      420                     425               430
    238 Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly
E--> 239           435                     440                     445
    240 Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys
E--> 241      450                     455                     460
    242 Ile Cys Gly Pro Asp Ser Ala Leu Ala Arg His Ile Gly Thr Asp Cys
E--> 243 465                     470                     475                     480
    244 Asp Ser Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro
E--> 245                      485                     490                     495
    246 Pro Ser Pro Thr Pro Gly Ser Thr Leu Thr Pro Pro Ala Val Gly Leu
E--> 247                      500                     505               510
    248 Val His Ser Gly
E--> 249           515
    288 <210> SEQ ID NO: 7
    289 <211> LENGTH: 132
    290 <212> TYPE: PRT
    291 <213> ORGANISM: Artificial sequence
W--> 292 <220> FEATURE:
    293 <223> OTHER INFORMATION: Partial amino acid sequence of human-originated soluble
    294       thrombomodulin
    296 <400> SEQUENCE: 7
    297 Met Leu Gly Val Leu Val Leu Gly Ala Leu Ala Leu Ala Gly Leu Gly
E--> 298   1               5                     10                     15
    299 Phe Pro Asp Pro Cys Phe Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro
E--> 300            20                     25               30
    301 Leu Asn Gln Thr Ser Tyr Leu Cys Val Cys Ala Glu Gly Phe Ala Pro
E--> 302          35                     40               45
    303 Ile Pro His Glu Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala
E--> 304      50                     55                     60
    305 Cys Pro Ala Asp Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro
E--> 306  65                     70                     75               80
    307 Glu Gly Tyr Ile Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu
```

misaligned amino acid numbers

P.6

RAW SEQUENCE LISTING   DATE: 07/23/2004
PATENT APPLICATION: US/10/501,671   TIME: 15:23:45

Input Set : A:\PTO.FG.txt
Output Set: N:\CRF4\07232004\J501671.raw   *misaligned amino acid 95 numbers*

```
E--> 308                    85                    90                    95
     309 Cys Glu Asn Gly Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly
E--> 310                   100                   105                   110
     311 Thr Phe Glu Cys Ile Cys Gly Pro Asp Ser Ala Leu Ala Arg His Ile
E--> 312         115                   120                   125
     313 Gly Thr Asp Cys
E--> 314         130
     334 <210> SEQ ID NO: 9
     335 <211> LENGTH: 21
     336 <212> TYPE: DNA
     337 <213> ORGANISM: Artificial sequence
     339 <220> FEATURE:
     340 <223> OTHER INFORMATION: Synthetic DNA for mutation
     342 <400> SEQUENCE: 9
     343 aatgtggcgg gcaagggccg a                                        21
E--> 349 1/12   delete
```

RAW SEQUENCE LISTING ERROR SUMMARY   DATE: 07/23/2004
PATENT APPLICATION: US/10/501,671   TIME: 15:23:46

Input Set : **A:\PTO.FG.txt**
Output Set: **N:\CRF4\07232004\J501671.raw**

Invalid Line Length:
The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:1; Line(s) 32
Seq#:3; Line(s) 146
Seq#:4; Line(s) 172
Seq#:7; Line(s) 306
Seq#:8; Line(s) 332

VERIFICATION SUMMARY
PATENT APPLICATION: **US/10/501,671**

DATE: 07/23/2004
TIME: 15:23:46

Input Set : **A:\PTO.FG.txt**
Output Set: **N:\CRF4\07232004\J501671.raw**

L:4 M:283 W: Missing Blank Line separator; <120> field identifier
L:8 M:270 C: Current Application Number differs, Replaced Current Application No
L:8 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:24 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:1
M:332 Repeated in SeqNo=1
L:123 M:254 E: No. of Bases conflict, LENGTH:Input:1440 Counted:1439 SEQ:2
L:123 M:320 E: (1) Wrong Nucleic Acid Designator, NUMBER OF INVALID KEYS:1
M:254 Repeated in SeqNo=2
L:125 M:252 E: No. of Seq. differs, <211> LENGTH:Input:1548 Found:1547 SEQ:2
L:136 M:212 E: (34) Invalid or duplicate Sequence ID Number, SEQUENCE ID NOS:3 differs:8
L:138 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:8
M:332 Repeated in SeqNo=3
L:185 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:5
M:332 Repeated in SeqNo=5
L:292 M:283 W: Missing Blank Line separator, <220> field identifier
L:298 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:7
M:332 Repeated in SeqNo=7
L:349 M:254 E: No. of Bases conflict, LENGTH:Input:12 Counted:22 SEQ:9
L:349 M:320 E: (1) Wrong Nucleic Acid Designator, NUMBER OF INVALID KEYS:2
L:349 M:252 E: No. of Seq. differs, <211> LENGTH:Input:21 Found:22 SEQ:9